

Metabolism and Dosimetry of ^{131}I

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A6.1. INTRODUCTION

The calculation of radiation dose to the thyroid gland from ^{131}I requires the assignment of numeric values to various biologic parameters that influence the concentration of the radionuclide within the thyroid. These parameters include the fractional uptake of iodine from the blood stream, the mass of the thyroid gland, and the retention of the radioiodine by the thyroid.

This report discusses the factors that alter the radioiodine concentration in the normal thyroid gland. Among the most important of these are: (1) the age of the exposed individual and the level of stable iodine in the diet, since they can considerably affect the size of the thyroid gland during growth and its function at all ages; (2) the dosimetric aspects of ^{131}I in the thyroid gland for normal human populations; and (3) estimates for thyroidal doses for various age groups per unit of assimilated radioiodine.

A6.1.1. The Iodine Cycle

Iodine-131, when incorporated into the body, follows the same pathway as the stable isotope of iodine, ^{127}I . Iodine, a required trace element, is a component of hormones produced by, stored within, and released into the blood from the thyroid gland. The thyroid hormones, thyroxine (tetraiodothyronine) and triiodothyronine, are required for normal growth, development, and metabolism.

Iodine in a water-soluble form, usually iodide, is readily absorbed into the blood from the gastrointestinal tract, lungs, and skin. Following oral administration, most, if not all, of the iodide is rapidly absorbed from the gut into the blood stream.

Circulating iodide is removed rapidly by both the thyroid and kidneys. Usually less than one-fourth of the plasma iodide is cleared by the thyroid gland, with about three-fourths cleared by the kidneys and excreted in the urine. One or two percent of the iodide is removed by the lactating female mammary glands. A small percentage of the iodide also is removed and recirculated by the salivary glands and gastric mucosa.

Iodide enters the thyroid's follicular cells from the blood mainly by active transport and is also available as a result of the de-iodination of organic iodine-containing compounds within the thyroid gland. The iodine concentrated by the thyroid gland is subsequently incorporated into iodotyrosines and iodothyronines (the thyroid hormones), which may be stored in the colloid of the thyroid follicles until required by the body.

Iodine uptake and thyroid hormone synthesis are regulated by a hormone of the anterior pituitary, thyroid stimulating hormone (TSH), the release of which is prompted by insufficient levels of circulating thyroid hormones and by thyrotropic releasing factor (TRF), secreted by the hypothalamus. When demands for thyroid hormone cannot be met by increasing the rate of hormone synthesis and secretion, an increase in the number and size of follicular cells and the size of the thyroid gland will result from TSH stimulation until the body's demands for thyroid hormones can be met.

A number of factors influence thyroid hormone production and utilization, such as age, sex and environmental temper-

ature. Other factors, such as the quantity of stable iodine in the diet, also influence the gland's function, and can markedly alter the uptake and retention of iodine by the thyroid, as well as the size of the thyroid. While these changes result from the homeostatic nature of the thyroid/pituitary/hypothalamic axis to maintain thyroid hormone production at an optimal level, these same changes can have an important influence on the radiation dose that results from the incorporation of ^{131}I into the thyroid gland.

A6.2. ANATOMY

The size of the normal human thyroid gland is dependent upon the age - and to a lesser extent, sex - of a person, and on the functional status of his or her thyroid, as determined by a number of dietary and physiological influences. Hence, the weight of the thyroid gland is highly variable.

The following section focuses on the "normal" thyroid size. In addressing the normal gland, however, a large fraction - perhaps the majority - of the data may be based upon thyroids that are not typical. Most of the available data originated as observations of mostly older hospitalized individuals, with, presumably, more abnormalities than a younger population.

A6.2.1. Influence of Age and Sex on Thyroid Size

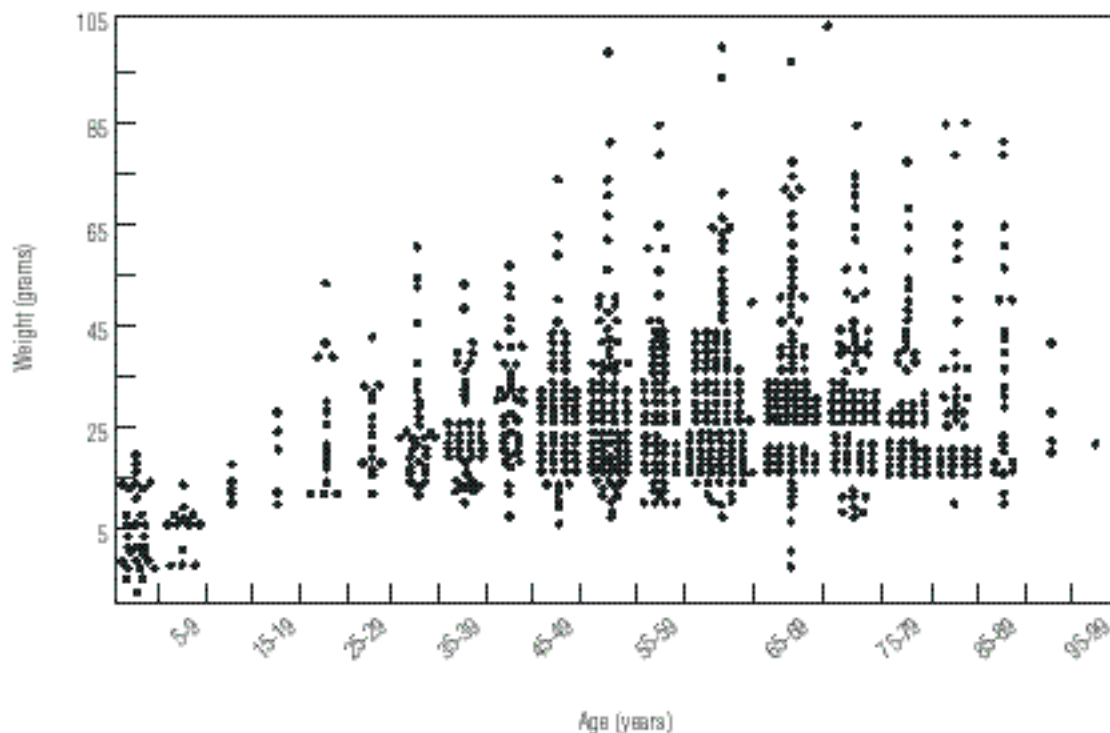
A6.2.1.1. Adult thyroid weight

Among the largest studies of clinically normal thyroid glands is a series of 821 thyroids obtained at routine consecutive autopsies of patients without clinical thyroid abnormalities at the Mayo Clinic from 1951 to 1953 (Mortensen et al. 1955). That study showed a wide scatter of individual weights at all ages (*Figure A6.1*), with some tendency for adult weights to increase with age (*Figure A6.2a*). The arithmetic mean of thyroid weights for people between 20 and 70 years of age graphically derived for the present report was about 29 g for men and 25 g for women. Mortensen et al. (1955) found no significant difference in thyroid weights of individuals residing in a goitrogenic versus a non-goitrogenic geographic area (*Figure A6.2b*).¹

One of the most detailed reports of the weight of the human thyroid is that of Mochizuki et al. (1963), who studied 762 normal thyroid glands, including and extending observations reported earlier (Eisenbud et al. 1962). Thyroid glands were obtained at autopsy from individuals who died suddenly and had no known history of thyroid disease. Dissections were performed within 24 hours after death, and thyroids were placed in preweighed plastic bags to prevent evaporation prior to weighing. The mean (\pm S.D.) weight of adult thyroids (over age 18) was 16.7 ± 6.9 g. In females, the thyroids weighed 14.9 ± 6.7 g, and in males, 17.5 ± 6.8 g. There was no apparent correlation between thyroid weight and body weight, height, or surface area.

Another study is that of Wellman (1969). The original report included 936 thyroid glands obtained at the University of Cincinnati Medical Center from 1961 to 1964. The glands were

¹ See Attachment (**Section A6.5**)

Figure A6.1. Scattergram showing relationship of age of patients to weight of thyroid gland. Redrawn from Mortensen et al. (1955).

collected at autopsy and immediately weighed and frozen and kept in a frozen state until time of dissection. At that time, the thyroids were reweighed and a correction was made for any amount of dehydration secondary to freezing. The thyroids were then “meticulously dissected” and only those thyroids that were grossly normal were included. All such thyroids were then compared with the results found previously at autopsy. After review of the microscopic sections and the prosectors’ descriptions, only 210 of the thyroids were thought to be normal and were included in the study. They found the mean (\pm S.D.) male thyroid weight to be 16 ± 5 g and the mean adult female thyroid weight to be 14 ± 5 g.

These data, with values from the literature compiled by Wellman et al. (1970), are given in Figure A6.3. The data from Mortensen et al. (1955), also shown in Figure A6.3, were derived by Wellman et al. by plotting the Mortensen et al. (1955) data as a population distribution taking the median value and applying a correction factor (80%) for nonthyroid tissue contributing to the measured weight (Attachment, **Section A6.5**). This resulted in a corrected median figure from the Mortensen et al. data of approximately 20 g for the adult thyroid weight.

Dunning and Schwarz (1981) reviewed the literature on thyroid weight measurements, including the series by Mochizuki

et al. (1963), and by Wellman et al (1970). On the basis of “255 single observations of adult thyroid mass from the literature combining both single observations and sample averages,” they estimated the adult (above age 18) thyroid weight to have a mean of 18.3 g (median of 16.5 g) and a range from 2 to 62 g.

The data summarized here are derived only from studies within the U. S., and obtained before 1965. Studies from other countries appear to provide somewhat higher weights (Agerbaek 1974; Hegedus et al. 1983; Rasmussen and Hjorth 1974). A study in Copenhagen (Hegedus et al. 1983) reported on the analysis of thyroid volume by ultrasound and validated the method by comparison to the volumes of the glands when surgically removed.² This study showed a mean thyroid volume of 18.6 ± 4.5 ml (male, 19.6 ± 4.7 and female, 14.7 ± 4.2 ml). The influence of body weight on the thyroid volume was 3 times greater than was that of age and explained the difference between the thyroid gland volumes of males and females solely by the difference in body weight. The values obtained in Copenhagen were lower than those measured by Agerbaek (1974) of presumably healthy accident victims in Jutland, Denmark, where a mean thyroid weight of 24.8 g (25.5 g for males and 22.9 g for females) was found. Here, no correlation

² The existence of more recent studies, especially those pertaining to anatomic data obtained from ultrasound examinations, is recognized. These data have been published subsequent to the preparation of the initial drafts of this appendix and are consistent with the analysis, results and conclusions presented herein.

Figure A6.2. Relationship of age and (a) sex and (b) geographic residence to weight of thyroid gland. Redrawn from Mortensen et al. (1955).

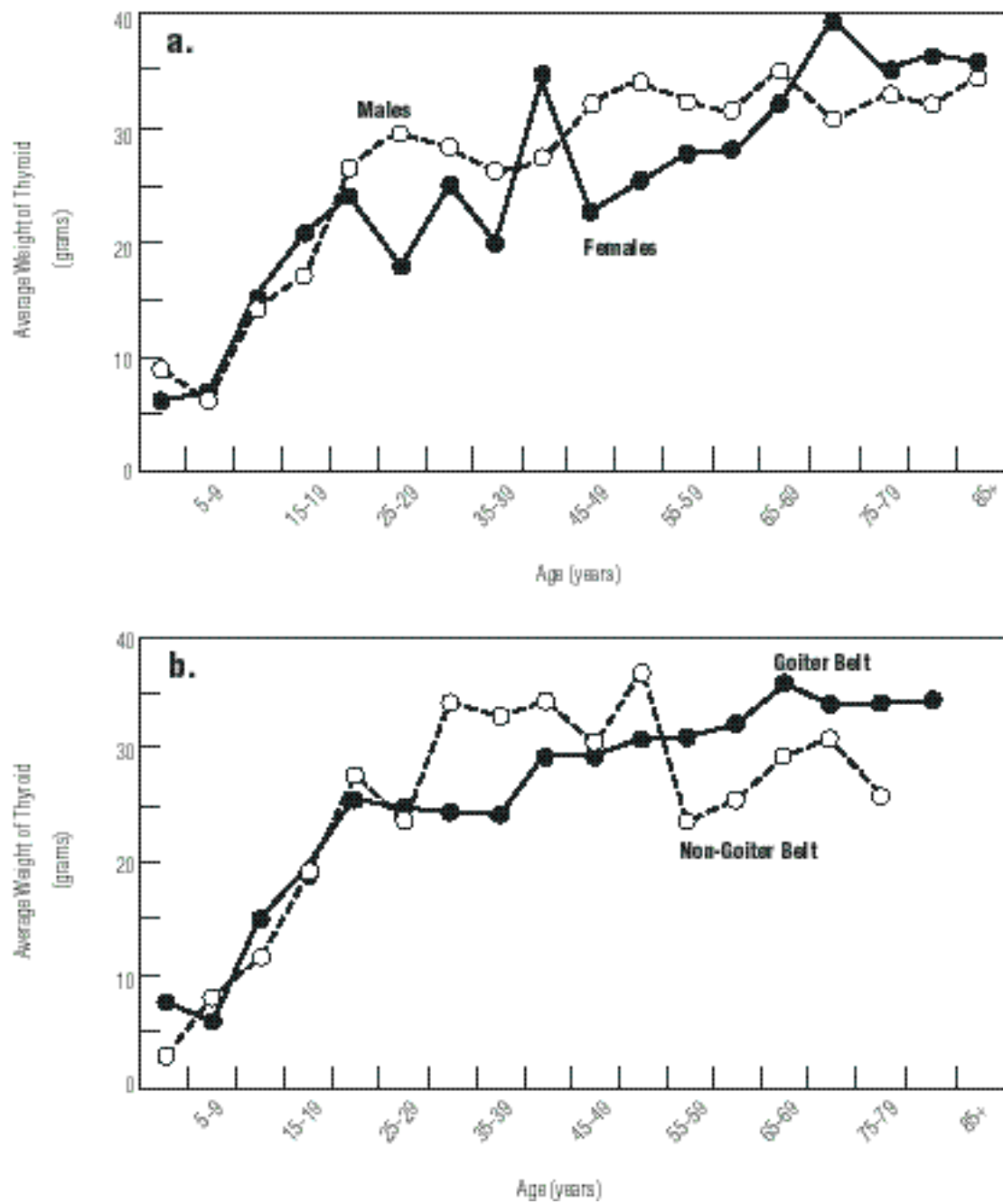
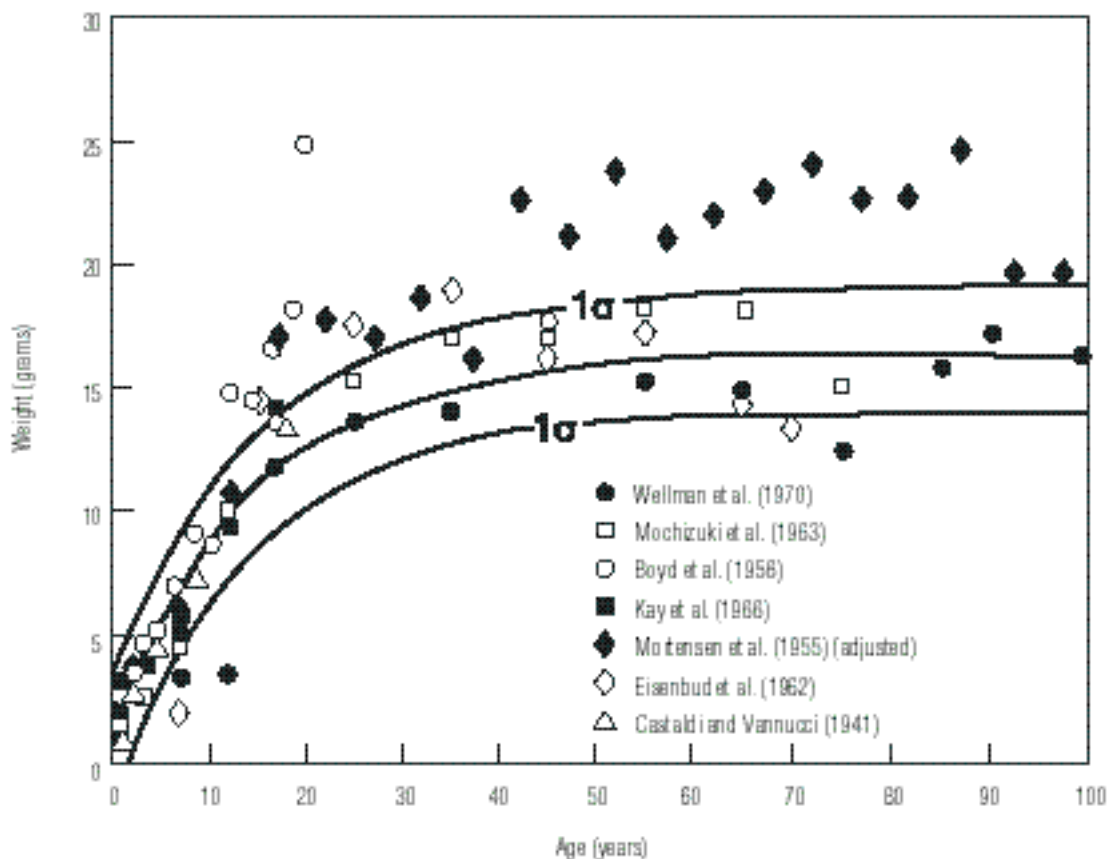


Figure A6.3. Thyroid gland weight as a function of age. Modified from Wellman et al. (1970).

with age was found, but a significant correlation with body weight was apparent in males. The median thyroid weight for the 156 males was 22.8 g, and for the 61 females, 19.3 g.

The ICRP (1975) in its Report of the Task Group on Reference Man suggests a reference adult male thyroid weight of 20 g and for adult female of 17 g. The 20 g weight was also given earlier as the standard adult thyroid weight (Spector 1956).

A6.2.1.2. Geographic variation

Because of the increased prevalence of goiter in the north and central U.S. early in this century, thyroids from individuals living in that region are generally believed to weigh somewhat more than those in the coastal areas. Kay et al. (1966) found thyroid weights of children in Rochester, Minnesota and Detroit, Michigan were significantly greater than those in eastern cities. However, the data of Mortensen et al. (1955), primarily from

older people, do not suggest a consistent geographical difference. In addition, thyroid weights from New York (Mochizuki et al. 1963) and Cincinnati (Wellman et al. 1970) are almost identical.

A6.2.1.3. Summary

The most striking characteristic of the measured thyroid weights appears to be the large variability in individual measurements (Figure A6.1). There is a general tendency for the gland weight in men to be slightly greater than in women (Table A6.1). Since in any individual the error of any weight estimate will be large, it appears reasonable to use a mean adult weight estimate of 17 g, with a value of 18 g for men and 16 g for women.

In some studies (Mochizuki et al. 1963; Mortensen et al. 1955), adult thyroid weights increased with age. In others, (Hegedus, 1983; Wellman et al. 1970), they did not.

A6.2.2. Thyroid Weight in Children

The most detailed study of thyroid weight in children is that of Kay et al. (1966), who studied 537 histologically normal glands of children through the age of 19. These glands were obtained from six hospitals across the U.S. The authors' analysis of the data did not indicate significant weight differences between male and female thyroids. The weights of glands from midwesterners were about 20% higher than easterners. They fitted their data by the method of least squares and derived the following expression for estimating thyroid weight for people up to age 19:

$$T = 1.48 + 0.054 \times A \quad (A6.1)$$

where:

T is thyroid weight in grams

A is age in months

Their formula also fits the data of Wellman, quoted by Kereiakes et al. (1972). The findings of Mochizuki et al. (1963) are also in general agreement (Figure A6.4 and Table A6.2).

A6.2.2.1. Fetal thyroid gland weight

The human thyroid gland begins its anatomic development near the end of the first trimester of gestation. Its functional development begins at the same time, as discussed below in Section A6.3.6.

An early study of human prenatal growth in the U.S. (Jackson, 1909) contained data on the fetal weights of 26 thyroid glands and the weights at term of 37 others. Their average weights ranged from 0.07 g in the fourth month to 3.4 g at birth.

The sizes of the thyroids in these studies were considerably larger than those reported later in the scientific literature, particularly in the later stages of gestation. The larger size probably reflects temporal and geographical differences in the iodine content of the diet.

Fetal thyroid weights were reported more recently by Eisenbud et al. (1963). These data were part of a larger body of

Table A6.1. Adult thyroid weight (U.S.), in grams

Reference	Male	Female	Mean
Mortensen et al. (1955)* 1951 - 1953 (Midwest)	29	25	28
Mochizuki et al. (1963) (±S.D.) (New York)	17.5 (±6.8)	14.9 (±6.7)	16.7 (±6.9)
Wellman (1969) (±S.D.) (Ohio)	16 (±5)	14 (±5)	
Wellman et al. (1970)			16
Dunning and Schwarz (1981) (recalculation of other published data)			18.3
Spector (1956) (review)			20
ICRP (1975) (review)	20	17	

* See attachment (Section A6.5)

Figure A6.4. Thyroid gland weight as a function of age for children.

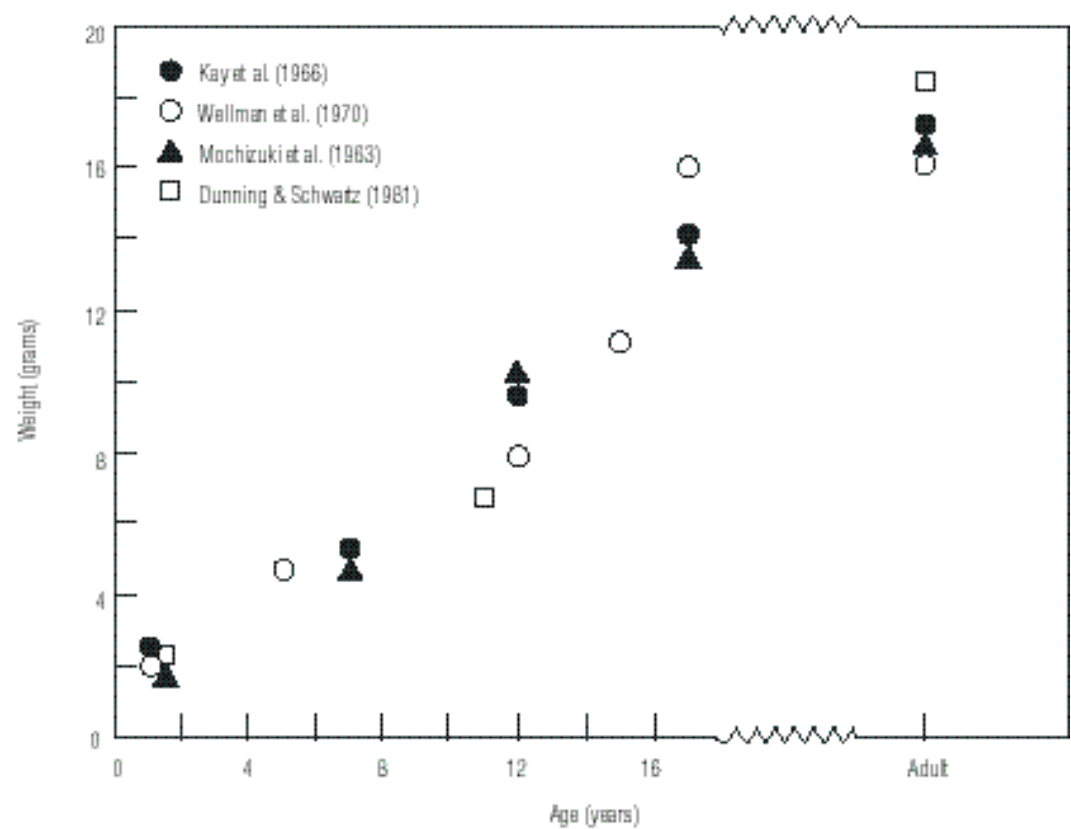
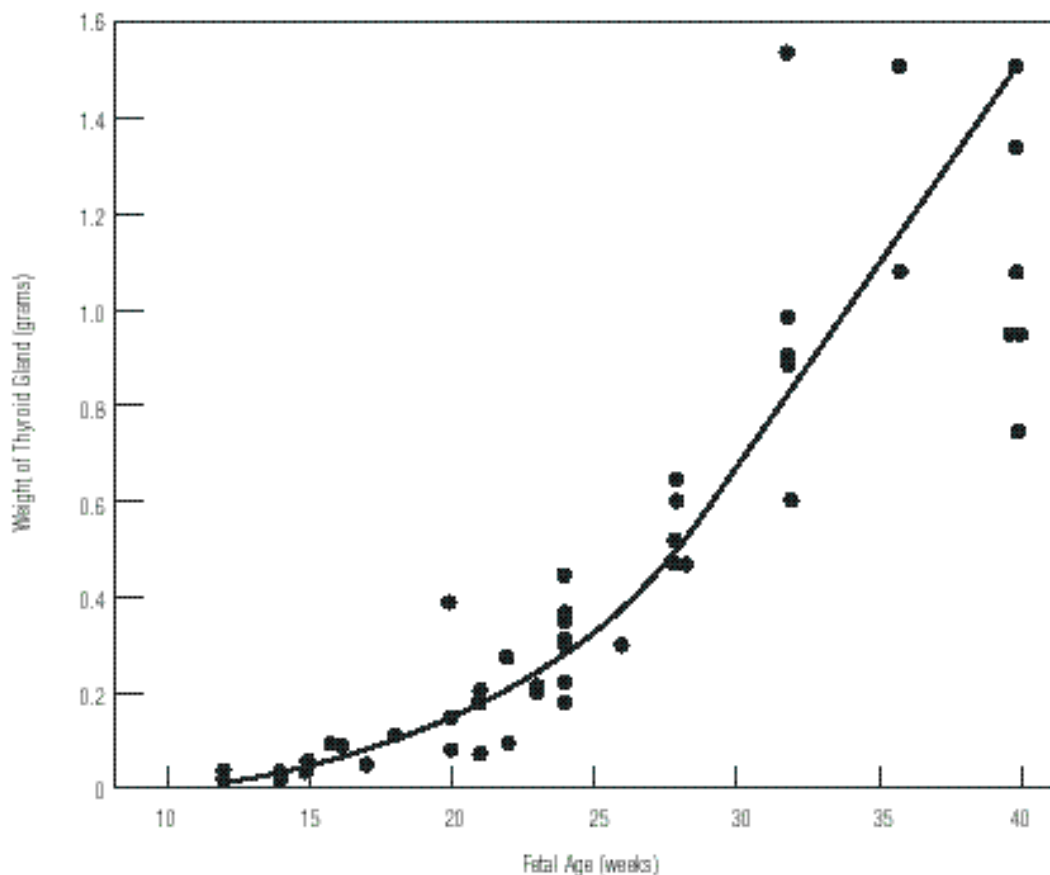


Table A6.2. Children's thyroid weights (grams) as a function of age

Reference	Age in Years								
	Newborn	1	0.5 to 2.0	5	4 to 10	10 to 14	15	6 to 16	15 to 19
Kay et al. (1966)(±SD)	1.5±0.7		2.6±1.4		5.3±2.1	9.6±5.1			14.2±5.2
Kereiakes et al. (1972)	1.5	2.2		4.7		8.0	11.2		16
Mochizuki et al. (1963) (±S.D.)	1.0±0.1	1.8±0.5	1.9±0.5		4.7±1.4	10.2±2.5			13.6±3.5
Dunning and Schwarz (1981)	1.4		2.3					6.7	

Figure A6.5. Thyroid gland weight as a function of fetal age. Data from Eisenbud et al. (1963) and Evans et al. (1967).



data on thyroid weights obtained at autopsy in New York City (Mochizuki et al. 1963). The values, obtained from 31 fetuses, ranged from 0.02 g at about 3 months to 1.5 g at full term.

Costa et al. (1965) reported the weights of 34 fetal thyroid glands obtained for an Italian study on maternal and fetal thyroid and pituitary function. Their weights ranged from 0.02 g at 12 weeks of gestation to 1.9-3.2 g at term.

Aboul-Khair et al. (1966) also reported the thyroid weights from 29 fetuses in Scotland. They found thyroid weights that ranged from 0.02-0.03 g at 13-14 weeks to up to 0.2 g at 20 weeks. The most mature thyroid (23 weeks) in their study weighed 0.17 g.

Evans et al. (1967) reported weights on 18 fetal thyroid glands in the U.S. Their thyroid weights ranged from 0.05 g at about 12 weeks to 0.7-1.5 g at term.

The combined American data (Figure A6.5) suggest a curve that departs from zero at 12 weeks of age. Midway through development, the fetal thyroid gland weighs about 0.12 g, increasing to about 0.6 grams by 30 weeks. At parturition, the thyroid gland weighs about 1.5 g.

A6.2.3. Influence of Thyroid Function on Thyroid Size

When thyroid hormone output from the thyroid gland is lower than required, the pituitary gland responds by releasing more thyrotropin (thyroid stimulating hormone, TSH). If the thyroid cells respond normally, a persistent increase in TSH causes them to hypertrophy and to increase in number, and thyroid gland enlargement results. Dietary iodine deficiency produces endemic goiter by this mechanism. A small goiter (about 2 or 3 times normal size) can occur when iodine intake is chronically below 20 μg per day (Stanbury et al. 1954; Wayne et al. 1964).

A6.2.3.1. Goitrogenic regions

In the past, iodine deficiency goiter was found across the northern U.S. and as far south as Nevada, Utah, and Colorado in the west, and Tennessee, Kentucky, and Virginia in the east (Figure A6.6). It disappeared from the U.S. before 1940, as evidenced by the low rate of goiter found in World War II recruits (0.06%) (Kelly and Snedden 1960). People who resided in these areas before 1940 might be expected to have larger than "normal" thyroid glands because of the prior iodine deficiency, although

normal function would be expected (Section A6.3.2.1).

Antithyroid substances in the diet, chemicals that interfere with hormone synthesis, are thought to exacerbate iodine deficiency goiter in some regions of the world, but firm evidence in support of this belief is lacking. Such substances may be responsible for small pockets of endemic goiter in the U.S. where iodine intake is adequate (e.g., in eastern Kentucky (London et al. 1965), and northern Virginia (Vought et al. 1967)). These goiters are small (enlarged by a factor of < 3), and the etiologic agent or agents have not been identified.

Iodine excess can cause goiter in susceptible individuals (Wolff 1969), and is known to cause endemic goiter in northern Japan (Nagataki et al. 1967). In the U.S., iodide goiter occurs sporadically and infrequently, and most often from medicinal treatment. It occurs when the plasma iodine level is above $20 \mu\text{g d}^{-1}$, a level much higher than is achieved even at the highest dietary intake encountered in the U.S.

A6.3. PHYSIOLOGY

A6.3.1. Incorporation of Radioiodine

Iodine-131 has three principal routes of entry into the body: ingestion, inhalation, and absorption through the skin.

Ingestion is the most important means of entry of ^{131}I present in the normal environment; inhalation and topical absorption are generally considered to be less important.

Generally one-fourth or less of the ingested ^{131}I is taken up by the thyroid gland. Peak uptake of ^{131}I in the thyroid usually occurs 1 to 2 days after ingestion. Under normal conditions, ^{131}I is lost from the thyroid gland with an effective half-life of about 1 week, where the effective half-life expresses the removal of ^{131}I resulting from physical decay and biological turnover.

Following inhalation of ^{131}I , the same partitioning of the radionuclide occurs, with less than one-fourth of the inhaled activity depositing in the thyroid gland. Some models for the metabolism of inhaled radioactivity suggest a slightly lower uptake for inhaled radioiodines than for ingested radioiodines. Because of the high solubility of iodine, however, it is reasonable to assume similar uptakes from both ingested and inhaled ^{131}I .

When ^{131}I is applied to the skin, it appears in the blood soon after application and is taken up by the thyroid gland, as with other modes of exposure. With topical exposures, however, the peak uptake is lower and later than occurs following oral administration of ^{131}I (as demonstrated in sheep (Wood et al. 1964)).

Figure A6.6. Geographic distribution of iodine-deficiency (shaded area) in the U.S. before 1940. Modified from Kelly and Snadden (1960) and Oddie et al. (1970).



Regardless of the mode of exposure, the actual uptake and retention of ^{131}I by the thyroid gland is determined by a number of intrinsic and extrinsic conditions, including the subject's thyroid hormone requirement, age and sex, and the iodine content of the diet. These have considerable influence on the behavior of the radionuclide within the body and on the subsequent radiation dose to the thyroid.

A6.3.2. Radioiodine Uptake and Retention

A6.3.2.1. Influence of dietary iodine

Considerable data exist concerning the intake of iodine in the U.S. and its influence on the fractional uptake of iodine by the thyroid gland. The dietary allowance of iodine recommended by the National Research Council (NRC 1989) is $150\ \mu\text{g d}^{-1}$ for adults and adolescents, and 40 to $120\ \mu\text{g d}^{-1}$ for younger children. This daily intake of iodine is associated with the absence of iodine deficiency goiter in a population.

In the steady state, iodine intake can be equated with urinary iodine excretion since only 10 to $15\ \mu\text{g d}^{-1}$ are excreted in the feces and much less is eliminated by other routes (Robbins et al. 1980). For the following discussion, iodine intake was evaluated from 24-h urinary iodine content, from the urinary iodine/creatinine ratio in random samples, from fractional uptake by the thyroid gland, and from food analysis.

Over the past several decades, dietary iodine intake has increased. Between 1940 and 1950, intake was about $150\ \mu\text{g d}^{-1}$, and between 1950 and 1960, it ranged from 150 to $250\ \mu\text{g d}^{-1}$ (Oddie et al. 1968a; Pittman et al. 1969). These data were obtained mainly in the northeastern states and to a lesser extent in the southeast and the Pacific Coast (California). From data obtained between 1963 and 1966, Oddie et al. (1970 and personal communication) estimated the geographic distribution of iodine intake in the country. The highest levels

(392 to $738\ \mu\text{g d}^{-1}$) were in the southwest and the lowest (238 to $391\ \mu\text{g d}^{-1}$) were in the northwest and northeast. The area including northern and central Nevada and Utah had iodine intakes in the middle to lower ranges (Figure A6.7). In southern Nevada and Utah in 1963 to 1966, iodine intake was relatively high (392 to $499\ \mu\text{g d}^{-1}$), and urine iodine measurements conducted in 1966-1967 gave a mean excretion of about $300\ \mu\text{g d}^{-1}$ (Rallison et al. 1974). In 1968 to 1970, a representative 10-state survey by the U. S. Public Health Service (Trowbridge et al. 1975a) showed the median urinary iodine/creatinine ratio to be $250\ \mu\text{g/g}$, with the highest levels above $800\ \mu\text{g/g}$; there was no iodine deficiency in any region. The calculated median iodine intake for a 60-kg adult, based on urinary creatinine of 0.025 g/kg body weight, is $375\ \mu\text{g d}^{-1}$. A four-state survey of children found the mean iodine excretion to be $443\ \mu\text{g d}^{-1}$ (Trowbridge et al. 1975b). Between 1974 and 1980, dietary iodine analysis by the Food and Drug Administration gave an estimated intake from food of 400 to $600\ \mu\text{g d}^{-1}$, and food analysis in 1963 indicated an average intake in both adults and children of about $400\ \mu\text{g d}^{-1}$ (Allegrini et al. 1983). To these values, "discretionary" intake from iodized salt (300 to $500\ \mu\text{g d}^{-1}$) should be added.

Based on these reports, iodine intake in the U.S. as a whole may be summarized as shown in Table A6.3. The estimate of $800\ \mu\text{g d}^{-1}$ for the median intake after 1970 based on food analysis may, however, be an overestimate, because fractional iodine uptake by the thyroid is usually higher than would be expected for such an intake level.

A6.3.2.2. Iodine uptake

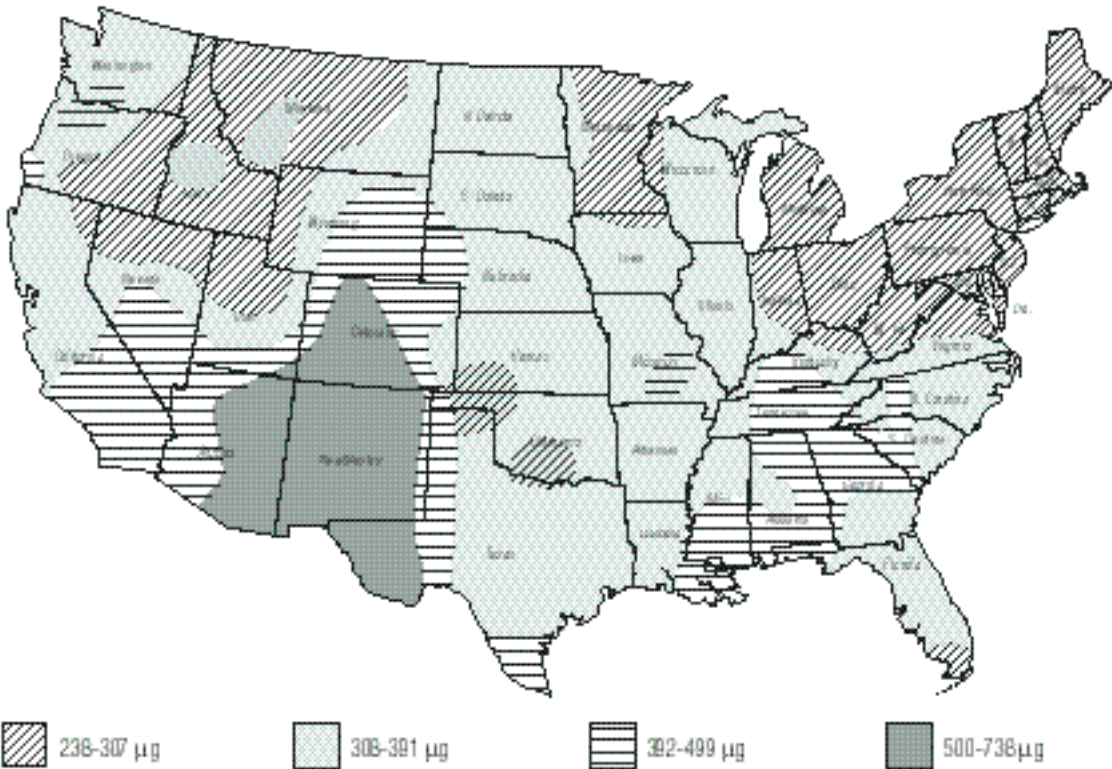
Since the evaluation of iodine intake has revealed wide deviations from the median for individual euthyroid persons, it is important to examine the effect of iodine intake on normal thyroidal iodine uptake. An acute short-term increase in iodine

Table A6.3. Dietary iodine intake in the U.S. in the past three decades.*

Years	Iodine Intake	
	Median ($\mu\text{g d}^{-1}$)	Range (% of the median)
1950-1960	200	– 20% to + 25%
1960-1970	375	– 35% to + 100%
1970-1980	~ 800	– 50% to + 38%

*See Section A6.3.2.1. for references

Figure A6.7. Geographical distribution of daily dietary iodine intake in the U.S. between 1963 and 1966, as derived from radioiodine uptakes and renal clearance rates. Modified from Oddie et al. (1970).



intake up to 2 mg d⁻¹, well within the dietary range, has no effect on the fractional uptake (Feinberg et al. 1959; Nagataki 1974; Oddie et al. 1967; Wagner et al. 1961; Wolff 1976). If the increased intake persists for more than several days, radioiodine uptake decreases (Saxena et al. 1962; Wagner et al. 1961) (Figure A6.8). Adjustment to a new steady level requires a period of 2 to 4 weeks (Wayne et al. 1964). An extensive study of North Americans and others on their usual diet has shown that the mean iodine intake derived from the fractional thyroïdal uptake agrees reasonably well with that derived from urinary ¹²⁷I excretion (Fisher et al. 1965; Oddie et al. 1970). This indicates that, on the average, North Americans are in iodine balance, although individuals may be in positive or negative balance at any point in time.

Therefore, it is reasonable to expect that the pool of ¹²⁷I will remain constant in the thyroids of subjects whose long-term average iodine intake is steady (although it may fluctuate from day to day), and that the fractional iodine uptake by the thyroid

will not vary with randomly fluctuating iodine intake. In such circumstances, when the average iodine intake is known, the fractional iodine uptake can be estimated from a model such as that described by Stather et al. (1983). Thus,

$$U = \frac{I}{D + R} \tag{A6.2}$$

where:

- U = fractional thyroid iodine uptake
- I = thyroid ¹²⁷I uptake rate = 60 to 70 µg d⁻¹
- D = dietary ¹²⁷I intake per day
- R = iodine recycled from the thyroid = 0.8 to 0.9 I.

Figure A6.8. (a) Measurements of accumulation of ^{131}I and ^{125}I by the thyroid and circulating iodide during the first 10 days of increased iodine intake in a euthyroid subject. Redrawn from Wagner et al. (1961).
 (b) Each dot represents the uptake of radioactive iodine by one child at the end of 2 weeks' administration of a given stable iodide level Redrawn from Saxena et al. (1962).

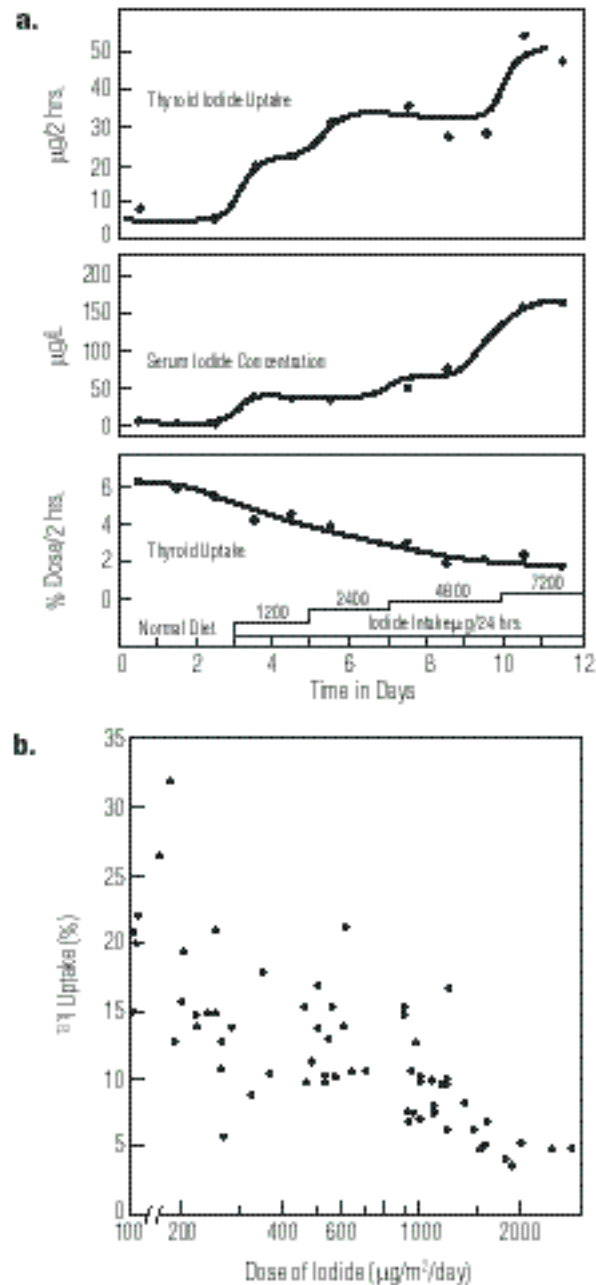


Table A6.4. Fractional iodine uptake by the adult thyroid, calculated from data in Table A6.3, and from equation A6.2*

Years	Fractional thyroid uptake	
	Median	Range
1950-1960	0.24	0.20 to 0.28
1960-1970	0.14	0.075 to 0.25
1970-1980	~ 0.071	0.052 to 0.13

*I = 60 $\mu\text{g d}^{-1}$, R = 0.8 l

From the intake data in Table A6.3, the thyroid uptake can be calculated (Table A6.4).

The estimated iodine uptake for 1970-1980 in Table A6.4 is unrealistically low, whereas that for 1960-1970 (14%) is in reasonable accord with that now existing in North America (Section A6.3.3.1), and that for 1950-1960 also agrees well with reported data.

A further consideration concerns the relation of dietary iodine intake to the retention of iodine by the thyroid gland. Studies in Japan, where a chronically high iodine intake exists (Nagataki et al. 1967), in Northern American children given up to 2 mg d⁻¹ (Saxena et al. 1962), and in North American adults given up to 100 mg d⁻¹ (Sternthal et al. 1980) have shown that the rate of secretion of thyroidal iodine is not inhibited at intake levels up to 10 mg d⁻¹ and is only slightly affected from 10 mg d⁻¹ to 100 mg d⁻¹. This conclusion is based on measurement of the rate of thyroxine degradation, the serum protein-bound iodine (PBI) level, and the serum TSH level in the three respective studies. In a normal individual, the amount of ¹²⁷I released from the thyroid is a constant 60-70 $\mu\text{g d}^{-1}$ (Robbins et al. 1980). The proportion of secreted ¹²⁷I that is recycled into the thyroid, however, varies with the fractional thyroid iodine uptake, and, hence, with the dietary intake (Stather and Greenhalgh 1983).

A6.3.3. Influence of Age and Sex on Radioiodine Uptake

Quimby et al. (1950) reported 24-h ¹³¹I uptakes based on over 1000 procedures from 1948-1950. They found mean uptakes to be 23.5% for males and 25.8% for females.

Before 1960, radioiodine uptake measurements varied considerably due to lack of adequate and appropriate technical standardization. By about 1960, standardized procedures devel-

oped at the Oak Ridge Institute of Nuclear Studies (Brucer 1957) gained wide usage, and resulted in more consistent and more reliable thyroid uptake data. In 1960, the International Atomic Energy Agency further clarified the radioiodine uptake technique and defined the standard neck phantom (IAEA 1962).

Despite these major improvements, individual differences were still found, with a wide normal range and considerable overlap in the range of observed values among different age groups. Measurements in Europe in general were about 50% higher than those in North America. The analysis in this appendix refers to uptake measurements made in the U.S., however.

Because of the dependence of iodine uptake upon iodine intake, considerable geographic variation in uptake exists even within the U.S., as discussed in Section A6.3.2.1. The considerable decrease in radioiodine uptake in the U.S. beginning in the 1960s has been attributed to a widespread increase in dietary iodine content (Pittman et al. 1969).

Pittman et al. (1969) studied 24-h uptakes in 63 euthyroid subjects in 1959 and reported a mean uptake of 28.6% \pm 6.57% and a normal range of 16% to 42%. Measurements with the same method in 1967-1968 showed that uptake had decreased to 15.4% \pm 6.8%. Blum and Chandra (1971) reported a normal thyroid uptake range of 20 to 45% in the 1960s. The study of Oddie and Fisher (1967) of many medical centers across the U.S. reported a mean normal uptake of 25.6% \pm 8.3%. Dunning and Schwartz (1981) recalculated data from a number of studies done prior to about 1975, and found a mean of 19% and a median of 17%, with an observed range of 8% to 46%. The median and the lower limit are in accord with the calculated values in Table A6.4 for 1960 to 1970.

Several studies have reported normal values for 24-h uptakes in the 1950s and 1960s to lie between 15% and 45%, with an overall range between 9% and 55% (Table A6.5). More recent studies (after 1970) have a normal mean uptake in the range of 15% to 20%.

Geographic variations in thyroidal iodine uptake are suggested by urinary iodine excretion data of Oddie et al. (1970). From their data, a mean uptake value of 14% can be calculated for the southwest, 16% for the Gulf states, 26% for the north-east corridor and 20% for the rest of the U.S.

A6.3.3.1. Sex differences

Most investigators have not found significant sex differences in the radioiodine uptake. Those that have been reported appear to be relatively small. Quimby et al. (1950) found slightly high-

er uptakes in females than males (25.8% compared to 23.5%). Oddie et al. (1968b, 1970) suggested that the iodine intake is about 35% higher in males than females, which would correlate with a lower uptake in males. This was also found by Ghahremani et al. (1971) reporting a 17.8% mean uptake in males and 21% in females, and by Robertson et al. (1975), who reported uptakes of 16.9% in males and 19.6% in females with an overall average of 18.2%.

A6.3.3.2. Influence of age

There is general agreement that radioiodine uptake decreases with age. Quimby et al. (1950) showed significant (but probably not clinically important) decreases in thyroidal uptake of ^{131}I with age.

The average values declined from 27% uptake at < 20

Table A6.5. 24-h thyroid radioiodine uptake in the U.S. as a function of age (before 1970). (Percent of orally administered dose, mean \pm SD, and range.)

Reference	Adults	Children (age in years)				
		Newborn	0.5 to 2	3	5 to 10	6 to 16
Van Middlesworth (1954)		69.7*				
Oliner et al. (1957)	32.7 \pm 7				28.2	31.7
Pittman et al. (1969)	28.6 \pm 6.5 15.4 \pm 6.8					
Ogborn et al. (1960)		20.3 \pm 8.5 (3-7 days)				
Fisher et al. (1962)		62 (37-82)** 72 (34-93)***				
Kearns and Philipsborn (1962)	41 (23-69)	75 (30-100)		30 (10-42)	34 (6-78)	31 (14-50)
Morrison et al. (1963)		70 (65-75)* 50 (35-60)****				
Van Dilla and Bulwyler (1964)	23.1		20			23
Cuddihy (1966)	22.5					
Oddie and Fisher (1967)	25.6 \pm 8.3					
Kereiakes et al. (1972)	27		27			
Dunning and Schwarz (1981)	19	47	39			47

* Intramuscular

** Intravenous

*** Premature infants

**** Oral

years of age to 22-23% uptake for persons over 60 years of age. In some series, values remained constant until age 40 (McGavack and Seegers, 1959) or 60 (Rosenberg, 1958), with uptake decreasing thereafter. Studies of an older population (Gaffney et al. 1962) showed that the 24-h uptake did not change significantly between 50 and 89 years of age. Wellman et al. (1970) in their review of the literature suggested that the uptake decreased with age, as did others (Oddie et al. 1960). However, they suggested that the primary effect was seen in the male, whereas in the female the uptake was constant until the menopause, when it decreased.

A6.3.3.3. Children

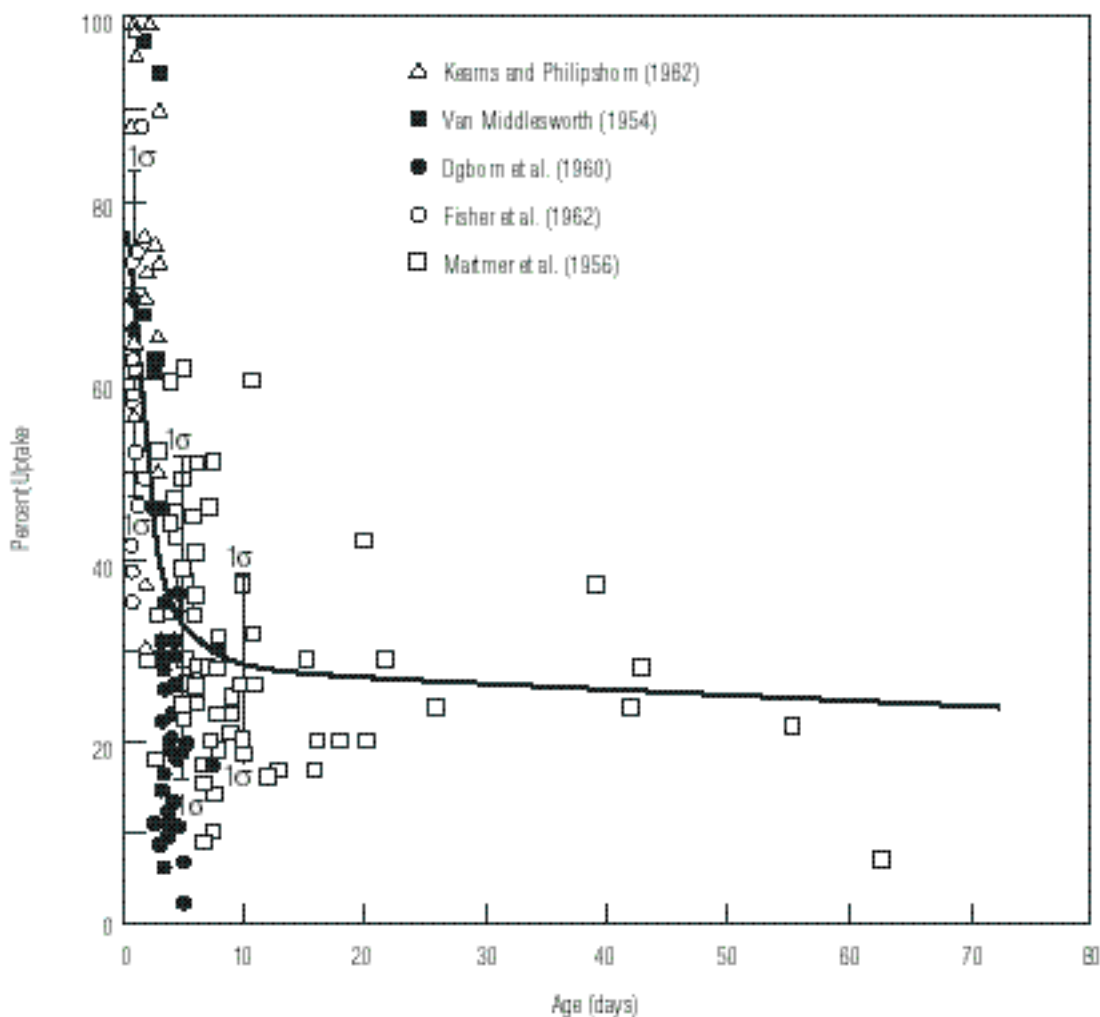
The thyroid gland is intimately involved with the processes of growth, development, and metabolism. Since those processes

change with age, the function of the thyroid also changes. Its function, in terms of iodine uptake by the gland and levels of circulating thyroid hormones, appears to be greatest immediately after birth.

Thyroidal uptake of ^{131}I in the newborn is markedly elevated. Uptakes of ^{131}I in seven 2- to 3-day-old infants 24 hrs after intramuscular injection ranged from 46% to 97% of the injected dose, with an average of 70% (Van Middlesworth 1954). Among 25 infants 0.5 to 2 days of age, thyroidal uptakes 24 hrs after intravenous injection ranged from 35% to 88% of the administered dose, with an average of 61%; by comparison, seven premature infants, 0.4 to 3 days of age, had average thyroidal uptakes of 73% of the injected dose, ranging from 46 to 100% (Fisher et al. 1962).

Similar results in 25 infants less than 1.5 days of age were

Figure A6.9. Thyroid uptake of ^{131}I as a function of age in the newborn.



obtained by Morrison et al. (1963). They found that the 24-h uptake by the thyroid was high, averaging 70 percent (17 infants) after intramuscular injection of ^{131}I . Uptake was lower when ^{131}I was administered orally, averaging 50 percent for eight infants.

The elevated ^{131}I uptake of the neonate is relatively short-lived, however. It decreases to “adult” values (Figure A6.9) by about 2 weeks of age (Wellman et al. 1970).

A6.3.3.4. Summary

Because of the wide range of individual iodine uptake values, any combined value can only be taken as a general population guide, and therefore estimates are of little value in any individual situation. While uptakes are relatively high in the first weeks of post-partum life, they decline soon to adult-like values. Most of the combined adult values are in the range of 20% to 30% (Table A6.5); this seems to be a reasonable estimate of the 24-h adult uptake prior to 1960. Since 1960, in the U.S., iodine uptake values have decreased with the concomitant increase in iodine intake, reaching the current mean uptake value of about 15%.

A6.3.4. Biologic Half-Life

For iodine, the biologic half-life characterizes the thyroid's turnover of iodine and its net release of hormone, reflecting loss from the gland and recirculation of released iodine back to the gland. A shorter half-life reflects a more rapid turnover.

The ICRP considered the biologic half-life for the adult thyroid to be 130 days (ICRP 1959) and later, 100 days (ICRP 1968). Stather and Greenhalgh (1983) in their proposed dose models selected 79 days for the adult, while Dunning and Schwartz (1981) in their combined value derived a mean of 85 days (median 72 days; range 21 to 372 days). Wellman et al. (1970), combining data from several studies, found a mean value of 68.1 days with a standard deviation of 30 days. Although Wellman et al. (1970) did not find a change in biological half-life with age, Cuddihy (1966) reported a somewhat faster turnover in children under 10 years.

There is general agreement that thyroids of children under 1 year have a considerably more rapid iodine turnover. Morrison et al. (1963) reported a rapid turnover (biologic half-life = 15 to 25 days) when tracer doses were given to newborn infants under 35 hours old. Dunning and Schwartz (1981) reported for newborn infants a mean biologic half-life of 16 days (median 13) and for children 6 months to 2 years, a mean of 13 days (median of 10). Adolescents approached the adult value with a mean of 50 days (median of 44), while the adult mean was 85 days (median 72 days). The ranges of observed values showed considerable overlap among the different age groups and there was no significant difference between the newborn and the 6 month to 2 year population. All other populations were significantly different to the 1% level.

A6.3.4.1. Summary

A thyroidal biologic half-life of 90 days is a conservative estimate for adults. Insufficient data are available to accurately characterize children, but figures of 15 to 20 days for newborns, about 20 days for children 1 to 2 years of age and 50 to 80 days for children under 10 years of age appear to be reasonable estimates (Table A6.6).

A6.3.5. Thyroidal Parameters in the Pregnant Woman

Thyroidal uptake of ^{131}I is increased in the pregnant woman from about the 12th week of gestation until a few weeks after parturition (Aboul-Khair et al. 1964; Halnan 1958; and Pochin 1952). Four hours after ^{131}I administration, thyroid uptakes (as indicated by the neck- thigh ratio of ^{131}I activity) were 3 to 4 times higher in pregnant than in nonpregnant women (Pochin 1952). Two hours after ^{131}I administration, neck-thigh ratios averaging 2 to 3 times the nonpregnant value were observed (Halnan 1958). Uptakes of ^{131}I 2.5 hours after administration averaged 30 to 35 percent throughout pregnancy, about 1.5 times the control (nonpregnant) value of 21 percent. Uptakes of ^{131}I 24 hours after administration were higher in pregnant women than in nonpregnant women by about 1.3, 1.6, and 2.0 times in the first, second, and third trimester, respectively (Ferraris and Scorta 1955).

The size of the thyroid gland apparently increases in pregnancy as well. Crooks et al. (1964) examined pregnant and nonpregnant women for visible and palpable goiters. They found that 71 percent of the pregnant women demonstrated mild, observable thyroid gland enlargement, while about 38 percent of the nonpregnant women did, for a ratio of about 2:1.

Few data exist on the release of ^{131}I from thyroid glands of pregnant women. It seems likely that the release of ^{131}I from the thyroid gland would be accelerated, since the processes acting to increase uptake and thyroid gland size will also influence retention values.

It should be noted that practically all these data are from Great Britain, where the dietary iodine intake generally has been lower than in the U.S. With higher dietary iodine levels, the increase in thyroid activity in pregnancy may be modulated or prevented.

A6.3.6. Thyroid Function in the Fetus

A convenient index for the expression of thyroidal radioiodine concentration by the fetus is the ratio of fetal thyroidal uptake to maternal thyroidal uptake. For determining the fetal/maternal (F/M) ratio of ^{131}I concentration, the uptake of each is given in terms of activity per unit of thyroid gland weight.

Some human data exist on the relative concentration of ^{131}I in maternal and fetal thyroid glands, indicating that the F/M ratio is very low during the first trimester of gestation and increases thereafter, exceeding unity in late gestation. For fall-out-derived ^{131}I , Eisenbud et al. (1963) found F/M ratios of 1.6 to 1.8 in three maternal-fetal pairs of thyroids, and 8.2 in a

Table A6.6. Biologic half-life of thyroid iodine (in days) as a function of age . (Mean \pm SD)

Reference	Adults	Children (age in years)				
		Newborn	1	0.5 - 2.0	10	6 to 16
ICRP (1975)	80					
Van Dilla and Bulwyler (1964)	108					
Rosenberg (1958) <50 y >50 y	92 \pm 17 63 \pm 4					
Stather and Greenhalgh (1983)	79		17		72	
Morrison et al. (1963)		15-25*				
Dunning and Schwarz (1981)	85	16		13		50
Saxena et al. (1962)			20		83	
Wellman et al. (1970)	68.1 \pm 30					
* Range						

fourth. Beierwaltes et al. (1963) reported an F/M ratio of 1.3 for a single pair of thyroids. Other studies using ^{131}I administered in a clinical setting (Aboul-Khair et al. 1966; Costa et al. 1965; Evans et al. 1967), wherein F/M ratios were obtained 1-2 days after maternal administrations of ^{131}I , reported ratios averaging about 1.2 at the end of the first trimester of pregnancy, 1.8 during the second trimester, and 7.5 for one thyroid pair in the third trimester, as estimated by Book and Goldman (1975).

Based on these data, and on a review of appropriate large animal data, Book and Goldman (1975) estimated F/M ratios over the entire gestation period. Ratios were lower for chronic exposures, about 1 and 2 for the second and third trimesters, respectively, ranging up to 3 in the latter, than for acute (single injection) exposures. For acute exposures, F/M ratios of about 3 (ranging from less than 1 to 7) and 5 (1 to 9) were midrange estimates for the second and third trimesters, respectively. The lower ratio for chronic exposures probably reflects a more complete labeling of the maternal gland and, hence, a larger denominator.

Although little information exists about the retention of ^{131}I by the fetal thyroid, that which is available clearly shows a more rapid release of the radionuclide from the fetal gland than from the maternal gland. From human fetal thyroids, Aboul-Khair et al. (1966) estimated biological half-times of 0.7 to 1 day for iodine from data obtained between the 13th and 19th

weeks of gestation. Data for late gestation are not available, but studies on guinea pigs, who, like people, have thyroids that begin to function early in gestation (Stara et al. 1966) indicate a more rapid ^{131}I turnover early in development than later (Book and McNeill 1975). Fetal guinea pigs in late gestation have a thyroidal iodine turnover approximately 4 times faster than their dams (Book 1977). Based on the human data for early gestation, and scaling from guinea pigs to people for later gestation, biologic half-times of 1, 10, and 20 days for human fetuses in early, middle, and late gestation, respectively, can be assumed.

A6.4. DOSIMETRY

A6.4.1. Uniformity of Dose

Radioiodine, when incorporated into the thyroid gland, is not distributed homogeneously throughout the follicles (Clayton 1953; Sinclair et al. 1956; Walinder 1972). Hence, radiation doses also can be inhomogeneously distributed, depending upon the energy of the emitted particle. Microdosimetric calculations pertaining to ^{125}I have suggested that the radiation dose to the follicular cell/colloid interface (where iodination occurs) is higher than the dose to cell nucleus (Gillespie et al. 1970; Greig et al. 1970; Vickery and Williams 1971), resulting from the low energy of its emissions that are consequently absorbed in close proximity to their origin. Van Best (1981, 1982) calculated

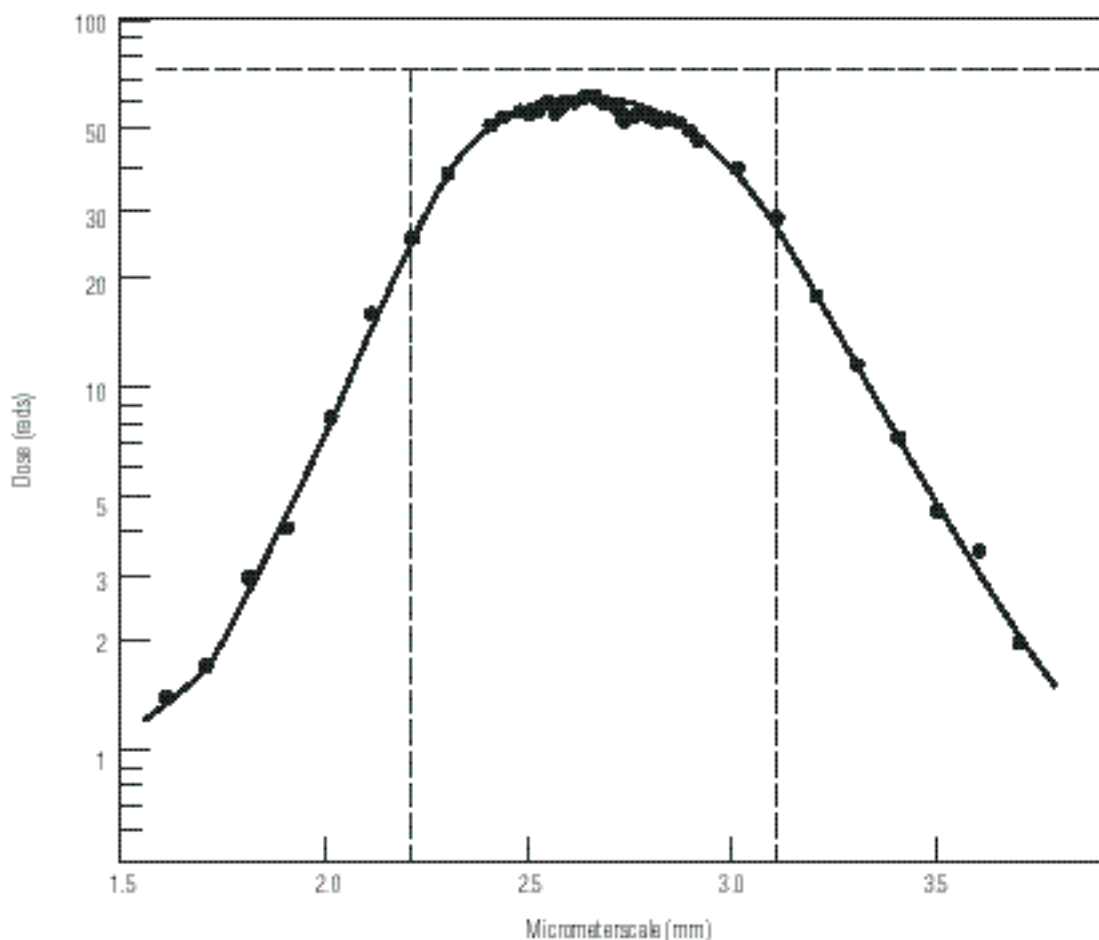
doses to thyroid follicular cells from several iodine isotopes, including ^{123}I and ^{125}I , which are of medical importance, and ^{131}I . His calculations showed the ratios between dose to the apical region of the cell and average thyroidal dose to be close to unity for ^{131}I , but relatively larger for ^{123}I and ^{125}I . From these and other published observations, it is evident that the intrafollicular dose variation, although important for iodine isotopes such as ^{123}I and ^{125}I , which have relatively weak emissions, is of little significance for ^{131}I .

The irradiation from beta particles from ^{131}I , can be considered to be fairly evenly distributed throughout the thyroid (Figure A6.10). Johnson and Myers (1983) indicated that in dose calculations the assumption of a homogeneous distribution

of a beta-emitting radionuclide is valid, provided that the range of the particles is much longer than the distance between the follicular lumina. Such is the situation for ^{131}I in the thyroid gland, where the range of the betas is almost 2000 micrometers (Quimby et al. 1970) and follicles in the adult have a diameter of 300 micrometers, including an epithelial cell lining of about 15 micrometers (ICRP 1975). The dose from ^{131}I to the nucleus of a follicular cell is the result not only of beta particles emanating from within its own follicular lumen, but also from the lumina of other follicles (Figure A6.10).

Based on the above, the calculations that follow assume that: (1) there is a uniform distribution of ^{131}I in the thyroid gland; and (2) that all of the energy is retained within the gland.

Figure A6.10. The beta dose in the median plane of a mouse thyroid lobe, showing the fall-off of the dose from the center of the lobe. The broken horizontal line denotes the doses in an infinite ^{131}I source with the same concentration of activity as that in the lobe, and the two vertical lines denote the edge of the mouse lobe (data from Walinder, 1971). Since the human thyroid lobe is many times larger than the mouse's, the fall-off at the edge represents a relatively much smaller part of the total dose.



For fetal thyroids, the calculated dose has been reduced to compensate for the loss of beta particles from the small glands (Quimby et al. 1970).

A6.4.2. Dose Calculations

For the calculation of the radiation dose to the thyroid gland from ^{131}I , equations utilize appropriate values for the energies of emitted particles and photons, the concentration of the radionuclide per gram of thyroid tissue, an expression for the retention of the radioactivity in the thyroid, and constants to relate the various dimensions.

As described by Quimby et al (1970), the standard radiobiological equation for calculating the dose from an internally deposited radionuclide, neglecting the dose accumulated during the period of uptake ($\sim 5\%$ of the total dose), is:

$$D_{\beta+\gamma} = C \times T_{\text{eff}} \times (73.8 \bar{E}_{\beta} + 0.0346 \tau \bar{g}) \quad (\text{A6.3})$$

where:

$D_{\beta+\gamma}$	the total dose from beta and gamma irradiation (rad),
C	the maximum concentration of the radionuclide in tissue ($\mu\text{Ci g}^{-1}$),
T_{eff}	its effective half-life (days),
\bar{E}_{β}	its average beta energy (MeV per disintegration),
τ	its specific gamma ray constant (R per mCi h^{-1} at 1 cm), and
\bar{g}	the average geometrical factor for the tissue or organ, equal to $3\pi r$ for spheres with radii (R) ≤ 10 cm.

The effective half-life, T_{eff} , is calculated from the equation:

$$T_{\text{eff}} = \frac{T_{\text{physical}} \times T_{\text{biological}}}{T_{\text{physical}} + T_{\text{biological}}} \quad (\text{A6.4})$$

where T_{physical} and $T_{\text{biological}}$ are the physical and biological half-lives, respectively.

In equation A6.3, the concentration of radioiodine has been assumed to be exponentially related to time, and all radiation is assumed to have been absorbed within the thyroid except in the case of the small thyroids of the fetus. As shown by Lee et al. (1979), these assumptions lead to overestimates of thyroid gland dose in the rat, with its relatively small gland.

For ^{131}I , the average beta energy, \bar{E}_{β} , is 0.18 MeV per disintegration and the specific gamma-ray constant, is 2.2 R per mCi per hr at 1 cm from a point source (Quimby et al. 1970). Whereas the physical parameters for Equation A6.3 are well defined, the biological components of the equation are not, and must be identified for each individual under consideration.

These are listed in Table A6.7, which summarizes information for different age groups presented in previous discussions.

A6.4.3. Dose Estimates

Doses to thyroid glands of various age groups are presented in Table A6.8. The highest dose per microcurie ingested is 33 rad per μCi for the newborn. The dose decreases with age until adulthood, when it is 1.6 rad per μCi ingested. For the elderly, the dose may be slightly lower. Fetal doses ranged from 0.1 rad per μCi administered to the mother in the 12th week of gestation to 6.9 rad per μCi near term.

The gamma-ray contribution to the total dose is small, amounting to only 3% of the dose in infants, rising to 6% in adults. In fetuses, the contribution of gamma-rays to the total dose is less than 2%. In most instances, given the uncertainties in the biological parameters used for dose calculations, the small gamma-ray component could be ignored.

Table A6.8 also includes values for the radiation dose in rad per microcurie present in the thyroid gland.

A6.4.3.1. Uncertainty evaluation

As has been demonstrated above, there is considerable variation in the anatomic and physiologic characteristics of the human thyroid gland. Therefore, an accurate description of any single thyroid is difficult, particularly in retrospect.

Even though the estimates of dose following ^{131}I ingestion (Table A6.8) represent best estimates for highly uncertain values, they are quite reasonable and realistic, based on available scientific data. Furthermore, the range of high and low estimates about these best estimates are relatively narrow, for the following reason: one may assume limits equal to 100 percent more or 50 percent less than the various biologic components of the dose equation (Table A6.7) to consider the influence of these parameters on the calculated dose. Hence, if the adult uptake were 12.5 or 50 percent of the administered dose, then the calculated dose would be 0.8 or 3.2 rad/ μCi , respectively, compared to the best estimate of 1.6 rad/ μCi . The same 0.8-3.2-rad/ μCi range would result from doubling or halving the thyroid gland size. Changing the biological half-life to 45 or 180 days, resulting in effective half-lives of 6.8 or 7.7 days, leads to doses of 1.5 or 1.7 rad/ μCi , showing the insensitivity of this term to large changes.

The largest underestimation of dose from the use of the 1.6-rad/ μCi adult value would occur when an individual's uptake and biological half-life are twice and thyroid size is half the assumed typical values, leading to a value of 6 rad/ μCi ingested. When these same biologic parameters are altered in the other extreme, a much smaller dose, 0.33 rad/ μCi , results. It must be recalled, however, that the three biologic parameters under consideration are interrelated. Conditions resulting in an increased iodine uptake, for example, may also result in an increased thyroid size and a decreased biological half-life; the

resulting interplay would offset the impact of each component of the dose equation on the calculation's outcome, and would tend to return the estimate toward the 1.6-rad/ μ Ci best estimate. For children, the range of uncertainty about the best estimates would be similar in magnitude to that presented for adults.

A6.5. ATTACHMENT

In a letter to Henry Wellman, dated April 1, 1966, J. D. Mortensen reported that in his study

... we did not meticulously dissect off all bits of thyroid tissue before we weighed them. Furthermore, the weight may be somewhat erroneous since the glands were weighed after storage in a formalin solution. They were not weighed accurately at the time of removal from the body.

Since Mortensen's main purpose was in evaluating thyroid nodules, he mentioned that they

...weighed most of the glands and did trim off most of the extra thyroid tissue that happened to remain with the glands but...did not make an accurate dissection of all bits of non-thyroid tissue and did not weigh with great accuracy. Our data as far as weight is concerned should not be considered very accurate scientifically.

Wellman, however, in his study of almost 1,000 thyroids dissected the glands "very meticulously to get accurate weights." By measuring before and after such dissection, Wellman felt that weighing the glands as Mortensen did "can overestimate the weight of the actual thyroid gland by about 20%." For a review article (Wellman et al. 1970), Wellman corrected Mortensen's data by applying a flat 20% factor (i.e., reducing weights by

Table A6.7. Metabolic and anatomic parameters for the calculation of radiation dose to the thyroid gland. Uptake and weight data are estimates for pre-1960 values. (See text for sources).

Age group	Parameter					
	Thyroid uptake (fraction)	Thyroid weight (grams)	Uptake/gram	Thyroid radius* (cm)	T _{biological} (days)	T _{eff} (days)
Adult	.25	17	0.015	1.27	90	7.3
Male	.23	18	0.013	1.29	90	7.3
Female	.27	16	0.017	1.24	90	7.3
Child						
15 y	.25	11	0.023	1.10	90	7.3
10 y	.25	8.5	0.029	1.00	80	7.1
5 y	.25	4	0.063	0.78	80	7.1
Infant (1 y)	.25	2	0.125	0.62	50	6.9
Newborn	.6	1.5	0.400	0.56	20	5.5
Fetus						
32 wk		0.8	0.085**	0.46	20	5.5
20 wk		0.15	0.051	0.26	8	4.0
12 wk		0.01	0.0085	0.11	1	1.0

* Radius for one sphere, with the assumption that the thyroid consists of two identical spheres of unit density.

** Uptake/gram for fetal thyroids are estimated from Book and Goldman (1975).

Table A6.8. Thyroid gland doses from 1 microcurie of I-131 ingested and from 1 microcurie of I-131 present in the thyroid. Data are based upon parameters presented in Table A6.7 for pre-1960 values.

Age group	Thyroid dose	
	Rad/ μ Ci ingested	Rad/ μ Ci retained in gland
Adult	1.6	6.4
Male	1.4	6.1
Female	1.8	6.8
Child		
15 y	2.5	9.9
10 y	3.1	13
5 y	6.6	26
Infant (1 y)	12	50
Newborn	33	55
Fetus*		
(32 wk)	6.9	100
(20 wk)	2.9	380
(12 wk)	0.1	1000

*See **Section 6.3.2**.

20%). The data presented by Wellman, and discussed in the text, represent “a non-parametric regression analysis” of all of the data in his tables and, therefore, the curve represents the mean of all the data Wellman presents.

It must also be noted that 50% of Mortensen’s thyroids were nodular. Their modularity is another factor that should be taken into consideration when interpreting his results. In Wellman’s series, all glands that were grossly and microscopically abnormal were eliminated, reducing the original 936 to 210.

Wellman (1969) “corrected” Mortenson’s data as a population distribution and pointed out that the weights were skewed to the high side. The log-normal distribution of thyroid gland weight has more recently been discussed by Dunning and Schwarz (1981). Wellman concluded that Mortenson’s data, even with a 20% correction, still were above the other data suggesting that they were probably influenced by the abnormal thyroids in their population (50%) and insufficient weight correction for non-thyroid tissue.

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